

REMARKS

Formal Matters

Claims 1-23, 26-28, and 30-31, as well as new claims 32-47, are pending after entry of the amendments set forth herein, of which Claims 26, 28, and 30 are withdrawn.

Claims 1-23, 27, and 31 were examined. Claims 1-23, 27, and 31 were rejected. No claims were allowed.

Claim 7 has been amended for clarity.

New claims 32-47 have been added. Support for new claims 32-47 can be found in the claims as originally filed and throughout the specification at, for example: claim 32: original claims 1 and 6, page 11, lines 4-15, page 12, line 18 through page 13 line 3; claim 33-38: page 21, lines 14-26; claim 39: page 11, lines 4-15; claim 40: page 24, line 38 through page 25, line 21; claims 41-46: page 21, lines 14-26; and claim 47: page 24, line 38 through page 25, line 7.

No new matter has been added.

Rejection Under 35 U.S.C. §112, first paragraph (Written Description)

Claims 1-5, 8-10, 12-23, 27, and 31 have been rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description. This rejection is respectfully traversed as applied and as it may be applied to the pending claims.

In making this rejection, the Examiner asserts on page 3 of the office action that "there appears to be no nexus between fluorescence and shared structure and function".

The law is clear that, if a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if not every nuance of the claims is explicitly described in the specification, then

the adequate written description requirement is met.¹ Further, "an applicant ...is generally allowed claims, when the art permits, which cover more than the specific embodiment shown."²

The Applicants maintain that the specification provides adequate written description support for such a disclosure. In particular, the Applicants respectfully submit that the specification provides abundant written description support for practicing the claimed invention. In particular, the Applicants note that the specification provides support for the subject nucleic acids at, for example, on page 8, line 11 through page 17, line 6; wild type and mutant proteins encoded by nucleic acids are described at, for example, on page 9, line 12 through page 12, line 15; exemplary methods of producing such mutants at, for example, on page 13 line 20 through page 14, line 8, and in greater detail on page 39, line 13 through page 57, line 5; resulting exemplary mutants at, for example, in Table 10 on pages 56-57; constructs, vectors, expression cassettes, and expression systems including the subject nucleic acids at, for example, on page 15, line 34, through page 20, line 33; and applications using the subject interconverted mutants at, for example, on page 32, line 4, through page 38, line 3.

Furthermore the specification provides working examples demonstrating exemplary protocols for isolating the subject nucleic acids encoding the proteins, exemplary mutagenesis protocols, and exemplary methods of generating and testing such mutant peptides (Examples I-VIII, pages 38-56), and examples of mutants generated (Table 10, pages 56-57).

In view of the above, it is submitted that the claims do comply with the written description requirement in that the claims are directed to nucleic acids encoding a chromo- or fluorescent protein from a non-bioluminescent Cnidarian species. The specification provides multiple representative examples, including working examples of

¹ *In re Alton* 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996).

² *Ethicon Endo-Surgery, Inc. v. United States Surgical Corp.*, 93 F.3d 1572, 40 USPQ2d 1019 (Fed. Cir. 1996).

representative nucleic acids encoding exemplary mutant proteins, such that one of skill in the art would have no doubt that the applicant was in possession of the invention as claimed at the time the application was filed.

Rejection Under 35 U.S.C. §102(b)

Claims 1-5, 8-10, 12-23, 27, and 31 have been rejected under 35 U.S.C. § 102(b) for allegedly being anticipated by Anderluh et al. (Biochem. Biophys. Res. Comm., 220:437-442 (1996)). This rejection is respectfully traversed as applied and as it may be applied to the pending claims.

All of the pending claims are directed to chromo- or fluorescent proteins. The term fluorescent protein is employed in its conventional, art recognized sense to refer to a protein having a plurality of residues that interact together as a fluorophore. See e.g., Chalifie et al., Science 263:802-805 (1994) (Exhibit A). **The art recognized definition of fluorescent protein does not include all proteins that include tryptophan residues that may give rise to residue intrinsic fluorescence.** The art recognized definition of fluorescent protein only includes proteins that have a fluorophore produced by the interaction of two or more amino acid residues working together.

The cited reference Anderluh et al., discloses cloning, sequencing, and expression of the wild-type Equinatoxin II protein from the sea anemone *Actinia equine*. The Office Action asserts that, as demonstrated in the prior research article published by the same group (Macek et al., Eur. J. Biochem., 234:329-335 (1995)), the protein is a fluorescent protein, wherein the fluorescence quality arises as a result of **intrinsic tryptophan residues** (Office Action, page 4).

However, the applicants respectfully disagree. The wild-type Equinatoxin II protein disclosed in the cited references is not a **chromo- or fluorescent protein**. The cited references disclose isolation and characterization studies of the Equinatoxin II protein with respect to pore formation and interaction of the toxin with lipid membranes. In particular, Macek et al. discloses results of conformational studies performed on the

wild-type Equinatoxin II protein using the well known method of quenching of intrinsic tryptophan fluorescence in order to examine protein folding and three-dimensional protein structure characteristics.

As such, Equinatoxin II is not a fluorescent protein, because any observed fluorescence is from individual tryptophan residues, and not from a fluorophore produced by the interaction of two or more amino acid residues. Therefore, Anderluh et al. and Macek et al. do not disclose a fluorescent protein, as defined in the present application and in the relevant art.

It is well established that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987), cert. denied, 481 U.S. 1052 (1987). See also, Scripps Clinic and Research Foundation v. Genentech, Inc., 18 USPQ 2d 1001 (Fed. Cir. 1991).

Since Anderluh et al. fails to teach nucleic acids encoding a **chromo- or fluorescent protein**, the cited reference fails to disclose every element found in the claims of the present invention. As such, Claims 1-5, 8-10, 12-23, 27, and 31 are not anticipated under 35 U.S.C. § 102(b) by the cited reference. Therefore, the Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. §102(e)

Claims 1-23, 27 and 31 have been rejected under U.S.C. § 102(e) for allegedly being anticipated by Tsien et al., U.S. Patent No. 6,342,379.

The 6,342,379 patent was filed as application serial no. 09/459,956 on December 13, 1999. The patent claims priority to an earlier application, i.e., "U.S. Pat. Ser. No. 08/765,860, now U.S. Pat. No. 6,107,066 filed May 8, 1997." However, the subject matter upon which the Examiner relies in making this rejection first appeared in the 09/459,956 application filed on December 13, 1999. Specifically, the Examiner bases

the rejection on Table 2, SEQ ID NO:5 and SEQ ID NO:6. A search of the parent 08/765,860 application finds this disclosure absent. In fact, there are no tables or sequence ID Nos. at all in the 08/765,860 application. This disclosure first appeared in the December 13, 1999 filing. Accordingly, the cited Tsien patent has a priority date of December 13, 1999, for this subject matter.

The present application is fully entitled to its claimed priority to application serial no. 09/210,330 filed on December 11, 1998. See the filed declaration by the inventors, of record. As such, U.S. Patent No. 6,342,379 patent does not qualify as prior art to the present application because U.S. Patent No. 6,342,379 has a priority date for the subject matter relied upon by the Examiner of December 13, 1999, over 1 year later than the priority date of the present application.

Since U.S. Patent No. 6,342,379 does not qualify as prior art to the present application, the rejection of Claims 1-23, 27 and 31 under 35 U.S.C. § 102(e) over U.S. Patent No. 6,342,379 may be withdrawn.

CONCLUSION

In view of the above remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: April 29, 2005

By: 

Bret E. Field
Registration No. 37,620

Enclosure:

Exhibit A: Chalifie et al., Science 263:802-805 (1994)

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

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